

CLAIMS

1. Compounds of the formula (I) and their pharmaceutically acceptable or technically applicable acid salts - where in the formula
 R^1 represents hydrogen, $C_{(1-4)}$ alkyl or $C_{(1-4)}$ alkoxy
 R^2 represents hydrogen, $C_{(1-4)}$ alkyl, carboxyl, $C_{(1-4)}$ alkoxycarbonyl, carboxamido, aryl or hetero-aryl
 R^3 represents hydrogen, $C_{(1-4)}$ alkyl, aryl-methylene, or aryl
Y is a valency bond, a straight or branched chain $C_{(1-4)}$ alkene, a carbonyl-amino- $C_{(1-4)}$ alkene, or a -S-
(CH₂)_m- group,
where all alkene groups above may be spaced by an arylene group,
n represents zero or the integer 1
m represents the integer 1, 2 or 3
Q represents hydrogen, hydroxyl or the oxygen radical (O[·]) or together with the N atom of the adjacent ring forms a +N=O (oxoimmonium) group
Z represents a single or double bond
and their pharmaceutically acceptable or technically useful salts.
2. Compounds according to claim 1 where the substituents contain C_{1-4} alkyl as alkyl, C_{1-4} alkoxy as alkoxy, C_{1-4} alkoxycarbonyl as alkoxycarbonyl, phenyl as aryl, piperidine, pyrrole or pyrrolidine groups as heteroaryl groups, a C_{1-4} alkene as alkene, 6 or 12 membered arylene as arylene groups in any of the substituents where such groups are mentioned.
3. The following compounds in either of their forms according to claim 1 and their salts formed with pharmaceutically acceptable or technologically useful acids:

- 2-(1-oxyl-2,2,5,5-tetramethyl-2,5-dihydro-1H-pyrrol-3-yl)-1H-benzimidazole 4-carboxylic acid amide radical
- 2-(2,2,5,5-tetramethyl-2,5-dihydro-1H-pyrrol-3-yl)-1H-benzimidazole 4-carboxylic acid amide
- 4-(4-carbamoyl-1H-benzimidazol-2-yl)-1-oxyl-2,2,5,5-tetramethyl-pyrrolidine 3-carboxylic acid methyl ester radical
- 4-(4-carbamoyl-1H-benzimidazol-2-yl)-2,2,5,5-tetramethyl-pyrrolidine-3-carboxylic acid methyl ester
- 2-(4-bromo-1-oxyl-2,2,5,5-tetramethyl-2,5-dihydro-1H-pyrrol-3-yl)-1H-benzimidazole 4-carboxylic acid amide radical
- 2-(4-bromo-2,2,5,5-tetramethyl-2,5-dihydro-1H-pyrrol-3-yl)-1H-benzimidazole 4-carboxylic acid amide
- 2-(1-oxyl-4-phenyl-2,2,5,5-tetramethyl-2,5-dihydro-1H-pyrrol-3-yl)-1H-benzimidazole 4-carboxylic acid amide radical
- 2-(4-phenyl-2,2,5,5-tetramethyl-2,5-dihydro-1H-pyrrol-3-yl)-1H-benzimidazole 4-carboxylic acid amide
- 2-[1-oxyl-2,2,5,5-tetramethyl-4-(3-trifluoromethyl-phenyl)-2,5-dihydro-1H-pyrrol-3-yl]-1H-benzimidazole 4-carboxylic acid amide radical
- 2-[2,2,5,5-tetramethyl-4-(3-trifluoromethyl-phenyl)-2,5-dihydro-1H-pyrrol-3-yl]-1H-benzimidazole 4-carboxylic acid amide
- 2-[4-(1-oxyl-2,2,5,5-tetramethyl-2,5-dihydro-1H-pyrrol-3-yl)-phenyl]-1H-benzimidazole 4-carboxylic acid amide radical
- 2-[4-(2,2,5,5-tetramethyl-2,5-dihydro-1H-pyrrol-3-yl)-phenyl]-1H-benzimidazole 4-carboxylic acid amide
- 2-(1,2,2,5,5-pentamethyl-2,5-dihydro-1H-pyrrol-3-yl)-1H-benzimidazole 4-carboxylic acid amide
- 2-(1-acetyl-2,2,5,5-tetramethyl-2,5-dihydro-1H-pyrrol-3-yl)-1H-benzimidazole 4-carboxylic acid amide

- 2 - (1-methoxy-2,2,5,5-tetramethyl-2,5-dihydro-1H-pyrrol-3-yl)-1H-benzimidazole 4-carboxylic acid amide
- 2 - [4-(dibenzofuran-4-yl)-1-oxyl-2,2,5,5-tetramethyl-2,5-dihydro-1H-pyrrol-3-yl]-phenyl]-1H-benzimidazole 4-carboxylic acid amide radical
- 2 - [4-(dibenzofuran-4-yl)-2,2,5,5-tetramethyl-2,5-dihydro-1H-pyrrol-3-yl]-phenyl]-1H-benzimidazole 4-carboxylic acid amide
- (1-hydroxy-2,2,6,6-tetramethyl-1,2,3,6-tetrahydro-pyridin-4-yl)-1H-benzimidazole 4-carboxylic acid amide
- 2 - (2,2,6,6-tetramethyl-1,2,3,6-tetrahydro-pyridin-4-yl)-1H-benzimidazole 4-carboxylic acid amide
- 2 - [4-(1-oxyl-2,2,5,5-tetramethyl-2,5-dihydro-1H-pyrrol-3-yl-methoxy)-phenyl]-1H-benzimidazole 4-carboxylic acid amide radical
- 2 - [4-(2,2,5,5-tetramethyl-2,5-dihydro-1H-pyrrol-3-yl-methoxy)-phenyl]-1H-benzimidazole 4-carboxylic acid amide
- 2 - [3-methoxy-4-(1-oxyl-2,2,5,5-tetramethyl-2,5-dihydro-1H-pyrrol-3-yl-methoxy)-phenyl]-1H-benzimidazole 4-carboxylic acid amide radical
- 2 - [3-methoxy-4-(2,2,5,5-tetramethyl-2,5-dihydro-1H-pyrrol-3-yl-methoxy)-phenyl]-1H-benzimidazole 4-carboxylic acid amide
- 2 - (5-oxyl-4,4,6,6-tetramethyl-4,6-dihydro-5H-thieno[2,3-c]pyrrol-2-yl)-1H-benzimidazole 4-carboxylic acid amide radical
- 2 - (4,4,6,6-tetramethyl-4,6-dihydro-5H-thieno[2,3-c]pyrrol-2-yl)-1H-benzimidazole 4-carboxylic acid amide
- 2 - (1-oxyl-2,2,5,5-tetramethyl-2,5-dihydro-1H-pyrrol-3-yl)-1H-benzimidazole 4-carboxylic acid isopropylamide radical
- 2 - (2,2,5,5-tetramethyl-2,5-dihydro-1H-pyrrol-3-yl)-1H-benzimidazole 4-carboxylic acid isopropylamide

- 1- (2,2,5,5-tetramethyl-2,5-dihydro-1H-pyrrol-3-yl-methyl)-1H-benzimidazole 4-carboxylic acid amide radical;
- 1- (2,2,6,6-tetramethyl-1,2,3,6-tetrahydro-pyridin-4-yl)-1H-benzimidazole 4-carboxylic acid amide.
- 2- (1-oxyl-2,2,5,5-tetramethyl-2,5-dihydro-1H-pyrrol-3-yl-methylsulphanyl)-1H-benzimidazole 4-carboxylic acid amide radical
- 2- (2,2,5,5-tetramethyl-2,5-dihydro-1H-pyrrol-3-yl-methylsulphanyl)-1H-benzimidazole 4-carboxylic acid amide
- 2- (1-oxyl-2,2,6,6-tetramethyl-1,2,3,6-tetrahydro-pyridin-4-yl-methylsulphanyl)-1H-benzimidazole 4-carboxylic acid amide
- 2- (2,2,6,6-tetramethyl-1,2,3,6-tetrahydro-pyridin-4-yl-methylsulphanyl)-1H-benzimidazole 4-carboxylic acid amide and its hydrochloric acid salt.
4. Compounds according to any of claims 1 to 3 in the form of their salts formed with inorganic or organic acids said salts being technologically useful such as oxalates or pharmacologically acceptable such as hydrochlorides, hydrobromides, sulphates, phosphates, phosphites, borates, lactates, ascorbates, acetates, fumarates, formates, tosylates, tartarates, maleates, citrates, gluconates, besylates etc.
5. Pharmaceutical compositions comprising as active ingredients in an effective dose of compounds according to any of the claims 1 to 9 or their pharmaceutically acceptable salts for the treatment of diseases which can be favourably influenced by PARP inhibition and/or scavanging oxidative stress.
6. Pharmaceutical compositions according to claim 5 comprising as active ingredients in an effective dose compounds

according to any of the claims 1 to 4 or their pharmaceutically acceptable salts for treatment of ischemia/reperfusion, inflammations and/or potentiation of cancer therapies.

7. Pharmaceutical compositions according to claim 5 or 6 which appear in formulations for oral, transdermal, parenteral, intramuscular, intravenous administration e.g. in the following forms: tablets, injections, solutions, suppositories, patches, suspensions etc.
8. Process for the preparation of compounds of the general formula (I¹) and their pharmaceutically acceptable or technically applicable acid salts - where in the formula
R¹ represents hydrogen, C₍₁₋₄₎ alkyl or C₍₁₋₄₎ alkoxy
R² represents hydrogen, C₍₁₋₄₎ alkyl, carboxyl, C₍₁₋₄₎ alkoxy carbonyl, carboxamido, aryl or hetero-aryl
R³ represents hydrogen, C₍₁₋₄₎ alkyl, aryl-methylene, or aryl
Y¹ is a valency bond, a straight or branched C₍₁₋₄₎ alkene, a carbonyl-amino- C₍₁₋₄₎ alkene,
where all alkene groups above may be spaced by an arylene group,
n represents zero or the integer 1
m represents the integer 1, 2 or 3
Q represents hydrogen, hydroxyl or the oxygen radical (O[·]) or together with the N atom of the adjacent ring forms a +N=O (oxoimmonium) group
Z represents a single or double bond
comprising reacting a carboxamide of the general formula (IV) - where
R¹ has the meaning as stated above -

with a heterocyclic derivative of the general formula (V) or (VI) - where

R², Y, Z and n have the meaning as stated above.

9. Process for the preparation of compounds of the general formula (IX) - where in the formula

R¹ represents hydrogen, C₍₁₋₄₎ alkyl or C₍₁₋₄₎ alkoxy

R² represents hydrogen, C₍₁₋₄₎ alkyl, carboxyl, C₍₁₋₄₎ alkoxy carbonyl, carboxamido, aryl or hetero-aryl

R³ represents hydrogen, C₍₁₋₄₎ alkyl, aryl-methylene, or aryl

where all alkene groups above may be spaced by an arylene group,

n represents zero or the integer 1

m represents the integer 1, 2 or 3

Q represents hydrogen, hydroxyl or the oxygen radical (O[•]) or together with the N atom of the adjacent ring forms a +N=O (oxoimmonium) group

Z represents a single or double bond

and their pharmaceutically acceptable or technically useful salts comprising

reacting a compound of the general formula VII - where

R¹ has the meaning as above -

with an alkylating agent of general formula VIII - where

R², Z, Q, n and m have the meaning as stated above and

X stands for a leaving group capable to react with the mercapto group to form a thioether

and optionally changing the substituents Q by way of oxydation and/or reduction to obtain the desired change in the substituents Q.

10. Process according to claim 9 where as a compound of formula VIII a correspondingly substituted alkyl-halogenide or alkyl-sulphonate is used such as any member of the group selected of the type alkyl chloride, alkyl bromide, alkyl-iodide, alkyl-mesylate, alkyl-tosylate, alkyl-triflate and the reaction is carried out in the presence of a base.
11. Process according to any of claims 8 to 10 *comprising* preparing any of the compounds of claim 1 to 7 in the form of its technologically useful salts such as oxalates or pharmacologically acceptable salts such as hydrochlorides, hydrobromides, sulphates, phosphates, phosphites, borates, lactates, ascorbates, acetates, fumarates, formiates, tosylates, tartarates, maleates, citrates, gluconates, besylates.
12. Method of treatment of diseases which are based on PARP activation or are caused by Reactive Oxidative Species (ROS) and Reactive Nitrogen Species (RNS) specifically cases of ischemia/reperfusion, inflammation, unfavourable reaction on the course of radiotherapy or chemotherapy by administration to the patient in need of such treatment an effective dose of at least one compound of the general formula I or its pharmaceutically acceptable salt - where in the formula
R¹ represents hydrogen, C₍₁₋₄₎alkyl or C₍₁₋₄₎alkoxy
R² represents hydrogen, C₍₁₋₄₎ alkyl, carboxyl, C₍₁₋₄₎ alkoxy-carbonyl, carboxamido, aryl or hetero-aryl
R³ represents hydrogen, C₍₁₋₄₎alkyl, aryl-methylene, or aryl

Y is a valency bond, a straight or branched chain C₍₁₋₄₎ alkene, a carbonyl-amino-C₍₁₋₄₎alkene, or a -S-(CH₂)_m-group,

where all alkene groups above may be spaced by an arylene group,

n represents zero or the integer 1

m represents the integer 1, 2 or 3

Q represents hydrogen, hydroxyl or the oxygen radical (O[•]) or together with the N atom of the adjacent ring forms a +N=O (oxoimmonium) group

Z represents a single or double bond

in the form of a dosage form comprising said effective dose.

13. Process for the preparation of pharmaceutical formulations which can be used for the treatment of diseases which are based on PARP activation or are caused by Reactive Oxidative Species (ROS) and Reactive Nitrogen Species (RNS) such as ischemia/reperfusion, inflammation, unfavourable reaction on the course of radiotherapy or chemotherapy by formulation of compounds of the general formula (I) or its salts - where in the formula
- R¹ represents hydrogen, C₍₁₋₄₎alkyl or C₍₁₋₄₎alkoxy
- R² represents hydrogen, C₍₁₋₄₎alkyl, carboxyl, C₍₁₋₄₎alkoxy-carbonyl, carboxamido, aryl or hetero-aryl
- R³ represents hydrogen, C₍₁₋₄₎alkyl, aryl-methylene, or aryl
- Y is a valency bond, a straight or branched chain C₍₁₋₄₎alkene, a carbonyl-amino-C₍₁₋₄₎ alkene, or a -S-(CH₂)_m- group,

where all alkene groups above may be spaced by an arylene group,

n represents zero or the integer 1

m represents the integer 1, 2 or 3

Q represents hydrogen, hydroxyl or the oxygen radical (O·) or together with the N atom of the adjacent ring forms a +N=O (oxoimmonium) group

Z represents a single or double bond

with usual additives into ready to use dosage forms by methods known per se.